of gametocytes to insure the infection of mosquitoes, and this is probably one of the reasons why mass treatment usually gives poor results.

The Commission repeatedly asserts that treatment with quinine can never be regarded as a *therapia sterilisans magna*. Knowledge of malaria now seems to be advancing after standing practically still for a number of years. This is attributed to the study of the biological aspects of the subject, while the discovery of effective synthetic antimalarial remedies has led to many experiments and to a promise of improvements in the treatment of the disease. A clear, and we believe useful, practical distinction is drawn between sporozoite therapy, which is called true causal prophylaxis, and clinical prophylaxis. For the first, it is the opinion that no drug is known which in harmless doses can be considered certainly effective. For the second, quinine is the most effective and best drug known, and daily doses of 6 grains are advised.

As far as the prevention of spread goes—and in this we are particularly interested—quinine and atebrin are effective in benign tertian and quartan, but against the gametocytes of malignant tertian (*Aestivo autumnal*) these drugs have only a feeble action. Plasmoquine has a powerful action against them, and it is recommended that it be given twice a week during the time when crescents are present in the peripheral blood. In badly infected areas (in Lagos, 90 per cent of the young children and 50 per cent of adults harbor malignant tertian parasites in their blood, and neighboring rural districts in all probability practically the entire population over 1 year of age, some 120,000 persons, carry malarial parasites in their blood continuously) it may become possible to substitute for present schemes of mass treatment a rational plan which will stop malaria from being fatal and mitigate its severity without interfering with the process leading to acquired immunity, which the Commission believes is most important to adult populations. In 1927, the Commission advised countries in which malaria was extremely prevalent to content themselves with the organization of their public health service on these principles, rather than to undertake such radical measures as are necessary for the complete elimination of the parasites.

REFERENCE

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NONSPECIFIC IMMUNITY BY HETEROLOGOUS VACCINATION

IMMUNITY is one of the most interesting as well as most important reactions of which we have any knowledge. Almost from time immemorial, it has been known that one attack of most contagious diseases protected from a second, generally throughout life. The first to theorize rationally on the subject and propose explanations of immunity was Pasteur, who discovered the first bacterial vaccine, when he found that attenuated cultures of the chicken cholera organism would protect against virulent ones. From that time on, experiments have been brought forward with confusing rapidity, and while we can say certainly that we know a good deal about immunity in general, and certain types of immunity in particular, there are still many points which remain to be clarified.

A recent piece of work is of more than usual importance. Armstrong and Harrison [1] have carried out experiments on a large number of animals immunized

against tetanus and botulinus, vaccine virus, and antityphoid vaccine, using normal saline injections as controls. After a proper period, these animals were injected with known fatal doses of diphtheria toxin-antitoxin, poliomyelitis virus, and cultures of *B. prodigiosus*. The general conclusion is that the various substances against which the animals were immunized exercised a subsequent protective action against the infectious and toxic agents used. The authors believe that this increased resistance is due to a " mobilization, strengthening and training of the defense mechanism." They recognize that increased resistance produced through heterologous immunization is only relative, and is not very strong, though they believe that the evidence indicates that it may be of value in modifying the course of such subsequent infections as poliomyelitis and postvaccinal encephalitis, as well as in increasing resistance to various subsequent infections.

In a review of the literature, it is pointed out that as early as 1893, Klein found that intraperitoneal injections of several varieties of bacteria would render guinea pigs refractory to known fatal doses of the same or other germs given from 8 to 12 hours later by the same route. These experiments have been confirmed by a number of observers, and some have even shown that preliminary intraperitoneal injections of various substances—bouillon, peptone, urine, etc.—would give a certain degree of immunity. In a few instances, the immunity against certain bacteria such as *B. cholerae,* was quite marked. The experiments cited include injections with yeast and with virulent tubercle bacilli, the latter of which were said to have rendered guinea pigs refractory to a certain extent against virulent anthrax. Vaccination against tuberculosis on a large scale, as carried out by Calmette with BCG, indicates that this nonspecific immunity notably reduces the general mortality of infants.

The increased protection by heterologous vaccines has been attributed to a cross-immunity, which is assumed and does not appear ever to have been proved. Armstrong and Harrison discredit this explanation on account of the great variety of substances which have been found capable of inducing increased resistance, and also the failure to find antibodies in the serum which show any cross-protection. They discuss also the fact noted in various camps during the World War, that recruits from rural areas were much more subject to infectious diseases than those who came from cities. An unusually striking instance of this was observed among two groups of Missouri recruits. The explanation in the majority of these cases seems clearly to be that urban dwellers are much more exposed to the ordinary so-called infectious diseases of childhood, but the point has been made by Love and Davenport that this would hardly account for the lowering in the incidence of such diseases as lobar pneumonia and cerebrospinal meningitis.

Long ago, Metchnikoff attributed such increased resistance to the breaking up of the phagocytes (phagolysis) and the setting free of cytase, at least as far as those cases in which some immunity is induced by intraperitoneal injections of bouillon. The general fact remains that as we grow older, we are apt to become less susceptible to certain infectious diseases, and this has been variously attributed to mild and unrecognized attacks or to vaccination by small, non-clinical, disease-producing infections. The whole matter is of extreme interest and importance, to which the contribution referred to has added valuable material.

REFERENCE

1. Armstrong, Charles, and Harrison, W. T. Heterologous Experience (Immunization) as a Factor in Resistance to Disease, *Pub. Health Rep.*, June 2, 1933, pp. 597–609.